Phosphoproteome Integration Reveals Patient-Specific Networks in Prostate Cancer.

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Public Summary:
We used clinical tissue from lethal metastatic castration-resistant prostate cancer (CRPC) patients obtained at rapid autopsy to evaluate diverse genomic, transcriptomic, and phosphoproteomic datasets for pathway analysis. Using Tied Diffusion through Interacting Events (TieDIE), we integrated differentially expressed master transcriptional regulators, functionally mutated genes, and differentially activated kinases in CRPC tissues to synthesize a robust signaling network consisting of druggable kinase pathways. Using MSigDB hallmark gene sets, six major signaling pathways with phosphorylation of several key residues were significantly enriched in CRPC tumors after incorporation of phosphoproteomic data. Individual autopsy profiles developed using these hallmarks revealed clinically relevant pathway information potentially suitable for patient stratification and targeted therapies in late stage prostate cancer. Here, we describe phosphorylation-based cancer hallmarks using integrated personalized signatures (pCHIPS) that shed light on the diversity of activated signaling pathways in metastatic CRPC while providing an integrative, pathway-based reference for drug prioritization in individual patients.

Scientific Abstract:
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